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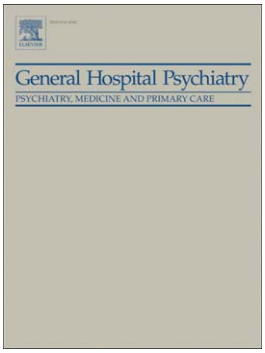

Hypersensitivity and Hyperalgesia in Somatoform Pain Disorders

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Hypersensitivity and Hyperalgesia in Somatoform Pain Disorders

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Hypersensitivity and Hyperalgesia in Somatoform Pain Disorders

Abstract

Objective: In psychiatry, pain disorders not explained by structural lesions have been classified for decades as *somatoform pain disorders*, the underlying concept being somatization. In a parallel move, somatic medicine has defined an expanding group of similar pain disorders, known as *functional pain syndromes*. Functional pain syndromes are characterized by enhanced pain sensitivity. The aim of our study was to investigate the proportion of patients with somatoform pain disorders who also meet the criteria of functional pain syndromes and the extent to which patients with somatoform pain disorders also show enhanced pain sensitivity.

Methods: Data on pain sensitivity in 120 hospitalized patients were obtained by means of two algometric methods. The group of patients with somatoform pain disorders was further divided into two subsets: patients with and those without a co-diagnosis of a functional pain syndrome. Patients with nociceptive pain served as control group.

Results: Of the 120 in-patients selected, 67 fulfilled the criteria of a somatoform pain disorder of which 41 (61%) also met the co-diagnosis of a functional pain syndrome. Patients with somatoform pain disorder differed from controls in that they showed enhanced pain sensitivity, irrespective of whether a functional pain syndrome was concomitantly present ($p<0.001$).

Conclusions: Somatoform pain disorders show considerable overlap with functional pain syndromes, including enhanced pain sensitivity. This suggests the relevance of integrating somatosensory aspects of pain into a modified understanding of somatoform pain disorders.

1. Background

For decades, pain disorders not or not adequately explained by structural somatic injury (or any other physiological processes such as inflammation) have been classified as *somatoform pain disorders* especially if they occur in the context of depression, anxiety disorders, or psychosocial stress. Under the DSM-IV section on somatoform disorders, somatoform pain disorder is defined as 'pain disorder associated with psychological factors' (307.80) [1]. In its definition of *'persistent somatoform pain disorder'* (F45.40), ICD-10 even explicitly attributed a *causal* significance to the psychological factors [2]. The rationale of DSM-IV and ICD-10 in categorizing somatoform pain disorders relies on the traditional concept of *somatization.* In the psychoanalytical theory, somatization was conceived as an experience of 'bodily symptoms' caused by (repressed) psychological distress. As a consequence, somatoform pain disorders were classified as 'mental disorders'. Patients, therefore, were referred to psychiatric care.

In a parallel move, somatic medicine defined an increasing group of so-called *functional somatic syndromes* [3,4] or, more specifically *functional pain syndromes* [5]. In 1990, The American College of Rheumatology, for instance, recognized *fibromyalgia* as a clinical entity. For the first time, hyperalgesia (with respect to the tender points) was proposed as a disease criterion for classifying patients with fibromyalgia [6]. Over the years, many additional functional pain syndromes were described. Different medical sub-disciplines focusing on their specialized area of medicine have defined their own specific functional pain disorders such as chronic temporomandibular joint disorders, irritable bowel syndrome, functional dyspepsia, chronic tension headache, chronic cardiac pain syndrome, chronic pelvic pain syndrome, etc. [5]. The predominant feature of these pain syndromes is hypersensitivity and hyperalgesia, either localized and/or generalized. In the past few years, these hypersensitivity disorders were also subsumed under the unifying concept of *central sensitivity syndromes* [7]. According to the definition of the International Association for the Study of Pain (IASP) [5], functional pain syndromes are characterized by precise anatomical localizations of pain (e.g. painful bladder syndrome), whereas in the definition of somatoform pain disorder such specific localization is absent. Neither of the pain categories is fully or partially explained by structural lesions. The essential difference between somatoform pain disorders and functional pain syndromes is the different emphasis laid on the underlying pathophysiology: psychological and emotional factors are considered as the main causative agents in somatoform pain disorders according to psychiatric

criteria, whereas in functional pain syndromes the emphasis is placed on the increased somatosensory/perceptive processing of stimuli [7]. Whereas hypersensitivity and hyperalgesia in functional pain disorders are well documented in many studies, there are only few studies about pain processing in somatoform pain disorders (**Table 1**).

It seems reasonable to assume, that both diagnostic systems are frequently engaged with one and the same phenomenology in the daily clinical routine. At least one can assume a considerable overlap between the two diagnostic approaches (**Fig 1)**. Therefore, it is not astonishing that e.g. the criteria of a 'high psychiatric comorbidity rate' or 'marked exposure to stress' have been described for many of the entities of functional pain syndromes, too [5]. The question of the extent to which enhanced pain perception (hypersensitivity, hyperalgesia) accompanies somatoform pain disorders is open. Owing to a traditionally psychogenic concept of somatization, the investigation of this 'somatic-sensory' aspect in somatoform pain disorders was neglected for a long time.

The aim of our study was to investigate the proportion of patients with somatoform pain disorder who also fulfil the criteria of functional pain syndromes and the extent to which patients with somatoform pain also show enhanced pain sensitivity. Our hypothesis was that in-patients with somatoform pain disorders would, on average, show a generalized increase in pain sensitivity (hypersensitivity and hyperalgesia) when compared to controls with pure nociceptive pain. Furthermore, we hypothesized that there would be no differences in pain sensitivity between the subgroups of somatoform pain disorder with and without a co-diagnosis of a functional pain syndrome.

2. Methods

2.1 Patients and Design

During a six-month period, we collected pain sensitivity data on 120 consecutive in-patients at a university hospital providing tertiary medical care. At our psychosomatic department we recruited patients with pain syndromes, all of whom fulfilled currently available diagnostic criteria for somatoform pain disorders (n=67). A further 53 patients with pure nociceptive pain attending the orthopedic department served as the control group.

The defining eligibility criterion for the diagnosis of a somatoform pain disorder was pain without a sufficient explanatory morphologic correlate, on the one hand, and concrete evidence for increased exposure to psychosocial stress, on the other (according to ICD-10 F45.40, ICD-10 F 45.41 and DSM-IV 307.80, respectively) [1,2]. Patients were examined by internal medicine residents trained in Engel's biopsychosocial interview technique [8] and supervised by board-certified internists and psychiatrists trained in psychosomatic medicine, including pain medicine. The interview included a standardized history with structured demographic and psychosocial data forms. In patients with a somatoform pain disorder, the treating physician made a diagnosis of a coexisting clinically relevant depressive disorder (termed henceforth "depression") based on ICD-10 criteria, current use of antidepressants, and/or a score >8 on the depression subscale of the Hospital Anxiety and Depression Scale (HADS-D) [9]. We did not apply the HADS-D scale in the case of an unequivocal diagnosis of depression.

The patient group with somatoform pain disorders was divided into two diagnostic subgroups: one with and one without a concomitant functional pain syndrome [5,10]. The group of functional pain syndromes comprised fibromyalgia syndrome, chronic tension headache, chronic temporomandibular joint disorder, chronic atypical facial pain, chronic low back pain syndrome, chronic atypical chest pain / cardiac pain syndrome, the group of functional gastrointestinal pain disorders (e.g. irritable bowel syndrome, functional dyspepsia, functional abdominal pain), and the group of chronic pelvic pain syndromes (e.g. chronic non-inflammatory prostatitis, painful bladder syndrome, and female urethral syndrome) [5,10].

At the orthopedic department we recruited a control group of patients with pure nociceptive pain as the primary clinical problem. Only patients with a clear peripheral correlate, verified by standard clinical and technical diagnostic methods (namely, X-ray, MRI or CT), were included. To limit potential confounding of somatic-nociceptive pain by overt psychological factors, orthopedic pain patients were excluded from the study if they were diagnosed with coexisting depression, currently used antidepressants, and/or had a HADS-D score >8. Patients with nociceptive pain disorders were divided into two subgroups: those with primary acute traumatic pain (e.g. accidents), and those with primary nociceptive pain of degenerative origin (e.g. degenerative joint disease).

All diagnoses were made by attending medical specialists according to currently employed criteria. In both departments all algometric and psychometric measurements were carried out by a fixed team of

two clinical research fellows. The study protocol was approved by the ethics committee of the Canton of Bern (Kantonale Ethikkommission Bern), Switzerland (No. 66/09).

2.2 Definitions, Instrumentation and Application

Pain perception characteristics were assessed with two algometric measurement methods. Both instruments have been validated and correlated in earlier studies [11]. Because absolute reference values do not exist for pain patients, hypersensitivity is defined relatively as a significantly lowered pressure pain detection threshold (PPdt) compared to the control group of patients with nociceptive pain ($p< 0.05$). Hyperalgesia is defined as significantly increased perception of a standardized nociceptive pain impulse compared to pain perception by patients in the control group with nociceptive pain ($p< 0.05$). It should be noted that this algometric procedure is intended to identify *generalized* increase in pain susceptibility. This implies a heightened experience of the perception of pain in the body as a whole.

The pressure pain detection threshold (PPdt) to determine hypersensitivity to pain was measured with a standard electronic algometer (Somedic Type II, size 161x170x30 mm, probe of 1.0 cm^2, Somedic Production AB, Hörby, Sweden) by bilateral testing on the middle fingers. The electronic algometer was calibrated following the standard protocol as recommended by the manufacturer and set to deliver a steadily increasing pressure (50 kPa for one second). In this method we checked for the threshold at which non-painful perception of pressure changes to painful perception in response to the gradually increased pressure applied. The patients press a button as soon as the pressure sensation subjectively turns into pain. Thereupon, the algometer freezes the value on the display. The procedure is repeated three times and the average value is used for data analysis. A one-minute break between each test procedure was planned in order to avoid local pain sensitization. Low thresholds correspond to high pain sensitivity.

The algometric measurement method to detect hyperalgesia was carried out by means of a pressure pain provocation test. For this type of algometry, we used a standardized peg with a clamping force of exactly 10 Newton at an extension of 5 mm (Type Algopeg, size 78x10 mm, polypropylene and nickel, spring reinforced in Switzerland, Annette Kocher, Inselspital Bern) [11]. The pressure is applied on the middle finger and the earlobes for 10 seconds each and is invariable. Patients tend to perceive the

pressure on their finger as being beneath or slightly above the pressure pain threshold. The pegs pressure exerted on an ear lobe is perceived as being consistently and clearly above the pain threshold [11]. The patient indicates the pain intensity on a numerical rating scale (NRS) on which 0 stands for 'no pain' and 10 for 'the most intense pain imaginable'. Since pain subjectively increases during the 10-second stimulation, patients were explicitly asked about the intensity of pain they perceived at the end of the test (i.e. at 10 seconds). High NRS values correspond with high pain sensitivity/hyperalgesia.

Both the electronic algometer and the peg algometer were applied to the nails of the middle fingers without touching the nail fold. Pain provocation tests with the peg algometer on the earlobe were performed on the central soft tissue part without touching the ear cartilage. We always administered the algometric tests to both sides of the body and used the average value of the measurements. All patients were also asked to rate their current mood with a NRS ranging from 0 ("excellent mood") to 10 ("worst mood imaginable"). The experiment was performed in a quiet setting without any interruptions and patients were shielded from other patients.

2.3 Data Analysis

For the statistical analyses we used SPSS 18 for Windows (SPSS Inc., Chicago, IL). Variables were expressed as percentages, mean values with standard deviation (SD) or standard error (SE) and, because some variables showed a skewed distribution, also as median plus interquartile range (IQR). The level of significance was set at $p<0.05$ (two-tailed). Algometric data were logarithmically transformed to obtain a normal distribution before performing group comparisons; however, for clarity all data are given in original units. We used the independent t-test and chi-square test, respectively, to compare continuous and categorical variables between two groups. To compare all four subgroups (somatoform with functional pain syndrome, somatoform without functional pain syndrome, nociceptive traumatic, nociceptive degenerative), we used the univariate general linear model, in which we controlled for age and gender. The internal comparison of the subgroups of somatoform pain disorders (with or without a co-diagnosis of a functional pain syndrome) were additionally controlled for depression, antidepressant use and mood, all of which may affect pain perception.

3. Results

3.1 Patient Characteristics

Patient characteristics are shown in **Table 2.** A total of 120 hospitalized patients were included in the study, out of which 67 patients met the criteria of a somatoform pain disorder. Forty-one (61%) of the 67 patients with a somatoform pain disorder had a clear co-diagnosis of an entity from the group of functional pain syndromes. Fifty-three patients with pure nociceptive pain served as controls (flowchart **Fig. 2**).

The vast majority of patients with a somatoform pain disorder had a diagnosis of coexisting depression and used antidepressants. Amongst patients with a somatoform pain disorder, depression was more often diagnosed in the subgroup with a co-diagnosis of a functional pain syndrome than in the subgroup without a functional pain syndrome ($p = 0.038$). The frequency of antidepressant use ($p = 0.49$) as well as current mood ($p = 0.77$) were similar in both these subgroups. Current mood was expectedly worse in patients with a somatoform pain disorder than in those with pure nociceptive pain ($p < 0.001$) as none of the patients with pure nociceptive pain was depressed per study criteria. The average age of patients in the subgroup of those with nociceptive pain of degenerative origin was higher than in the other three subgroups (p-values < 0.001). Women were more frequently affected with somatoform disorders than men, meaning that more men than women suffered from nociceptive pain ($p = 0.003$).

Functional pain syndromes included fibromyalgia (n=23), chronic low back pain (n=10), functional gastrointestinal pain syndromes, e.g. irritable bowel syndrome, functional dyspepsia, and functional abdominal pain (n=8), chronic tension headache (n=5), chronic temporomandibular pain (n=2), and atypical facial pain (n=1). Seven of the 41 patients had more than one co-diagnosis out of the group of the functional pain syndromes. The remaining 26 patients with somatoform pain disorders not corresponding to a specific co-diagnosis of functional pain syndromes all suffered from pain syndromes with regionally accentuated musculoskeletal pain, not fulfilling the criteria for fibromyalgia (according to ACR criteria 1990).

The control group of 53 patients with nociceptive pain included 27 with acute traumatic pain and 26 with degenerative osteoarthritic pain. Acute traumatic pain included lesions of the shoulders (n=6),

upper extremities (n=5), bone fractures or joint lesions of the lower extremities (n=16) as well as thoracic (n=2), vertebral (n=3) or pelvic traumas (n=2). Degenerative nociceptive pain included hip arthritis (n=9), knee arthritis (n=10), degenerative shoulder pain (n=5), and degenerative low back pain (n=10). In 15 of the 53 patients, nociceptive pain was located in more than one anatomical region (e.g. polytrauma and degenerative polyarthritic pain, respectively).

3.2 Pain Sensitivity Data

The pain sensitivity data without adjustments for covariates are shown in **Table 3.** With respect to hypersensitivity the measurements performed in patients with somatoform pain disorders with the electronic algometer revealed significantly lower pressure pain thresholds (PPtd) compared with the control group of patients with pure nociceptive pain ($p < 0.001$). The mean difference was -65.0 kPa (95% CI:-96.6 to -33.4). With regard to hyperalgesia, pain provocation tests in patients with somatoform pain disorders by means of the peg algometer consistently showed increased NRS values compared to controls with nociceptive pain ($p < 0.001$). For finger measurements, the mean difference was 2.5 (95% CI: 1.8-3.3) and for earlobe measurements 3.1 (95% CI: 2.3-3.8).

Subgroup comparison of patients suffering from somatoform pain disorder with or without a co-diagnosis of a functional pain syndrome did not reveal any significant group difference for any of the three pain sensitivity measures (p-values >0.25). Specifically, for the hypersensitivity test on the finger, the medians were 149.4 in the subgroup with functional pain syndromes, and 157.5 in the subgroup without functional pain syndromes (mean group difference = -8.1, 95% CI: -55.2 to 38.9). Concerning the hyperalgesia test on the finger, the medians were 4.6 for the subgroup with functional pain syndromes, and 3.6 for the subgroup without functional pain syndromes (mean group difference = 1.1, 95% CI: -0.3 to 2.5). For the hyperalgesia test on the earlobe, the medians were 7.4 in the subgroup with functional pain syndromes, and 7.0 in the subgroup without functional pain syndromes (mean group difference = 0.5, 95% CI: -0.8 to 1.7).

Adjustment for age and gender maintained the nonsignificant group difference (p-values >0.43) as did additional controlling for depression and use of antidepressants (p-values >0.20). Controlling for age, gender, and current mood (instead of depression and antidepressant use) did also not yield any

significant difference in pain sensitivity measures between the two subgroups of somatoform pain disorders (p-values >0.34).

In patients with pure nociceptive pain, the subgroup with traumatic pain showed lower hypersensitivity ($p = 0.013$) than the subgroup with degenerative pain (mean group difference in the pressure pain threshold (PPtd) = 52.4, 95% CI: 11.5-93.2), whereas hyperalgesia tests on the finger ($p = 0.13$) and earlobe ($p = 0.12$) showed no significant group difference. After controlling for age and gender, hyperalgesia on the finger was greater in the degenerative pain group compared to the traumatic pain group ($p = 0.34$), whereas hyperalgesia on the earlobe ($p = 0.14$) and hypersensitivity ($p = 0.23$) showed no group difference.

A comparison of all four subgroups using the univariate general linear model controlling for age and gender showed significant differences in all pain sensitivity measures between each of the subgroups with somatoform pain disorders versus the subgroup with traumatic nociceptive pain (p-values < 0.008, **Fig. 3a-c**). In contrast, hypersensitivity (**Fig. 3a**) was not different between each of the subgroups with somatoform pain disorders and the subgroup with degenerative nociceptive pain (p-values > 0.10, **Fig. 3a**). Except for the comparison of finger hyperalgesia between the somatoform pain disorder subgroup without a functional pain syndrome and the degenerative nociceptive pain subgroup ($p > 0.08$, **Fig. 3b**), all other hyperalgesia measures differed between the subgroups of somatoform pain disorders versus the subgroup with degenerative nociceptive pain (p-values < 0.004, **Fig. 3b, Fig. 3c**).

4. Discussion

The test arrangement adopted was used to investigate the trait of enhanced pain sensitivity in patients with somatoform pain disorders. The results obtained confirm our hypotheses: Firstly, a substantial proportion (61%) of patients with somatoform pain disorders also fulfils the criteria of a functional pain syndrome. Secondly, patients with somatoform pain disorders show an intensified pain perception associated with hypersensitivity and hyperalgesia compared with patients with nociceptive pain. The enhanced pain sensitivity in patients with somatoform pain disorder was independent of the concomitant presence of any functional pain syndrome.

Whereas studies on pain sensitivity in somatoform pain disorders are rare, evidence according to which functional pain syndromes are characterized by hypersensitivity and hyperalgesia has been corroborated by numerous studies in the past few years [5,7]. This is the first study using objective measures of pain sensitivity in a cohort of patients with somatoform pain disorder regarding the concomitant presence of a functional somatic pain disorder. However, we acknowledge that because our somatoform pain disorder patients were in-patients, the present results may not be generalizable to all patients with somatoform pain disorders. Furthermore, there were inevitable differences between the compared groups on depression rating, duration of pain, and antidepressant use. Also, our control group included patients with nociceptive pain of degenerative and traumatic origin. Subgroup analyses suggested that those with degenerative nociceptive pain might differ in pain processing from those with traumatic nociceptive pain to the extent that the former subgroup did not significantly differ in some pain sensitivity measures from the group with somatoform pain disorders.

There are many psychological influences on pain processing (e.g. stress, anxiety, depression, negative and positive mood) [12]. For instance, depression is independently associated with a reduced pain threshold [13]. A recent study, which examined pressure pain thresholds in similar patients, revealed that sensitivity to pressure was associated with depression, but not with multiple somatoform symptoms [14; Table 1]. Our subgroup comparison (somatoform pain disorder with or without a co-diagnosis of a functional pain syndrome) suggested no difference in hypersensitivity and hyperalgesia after controlling for depression, antidepressant use, and mood.

The high percentage of patients with somatoform pain disorders that meet a co-diagnosis of a functional pain syndrome confirms the assumption that there is considerable overlap between these two diagnostic categories. Considering that there is enhanced pain perception as a major common trait, the question arises as to whether somatoform pain disorders and functional pain syndromes are not one and the same disease group from which two distinct diagnostic aspects are picked and emphasized. Have we witnessed two parallel diagnostic coding systems establishing themselves over the past decades?

Regarding the question as to the extent to which the categories of somatoform pain disorders and functional pain syndromes overlap, we are aware that our study focuses on functional pain syndromes within somatoform pain disorders only. Vice versa - the quota of somatoform pain in functional pain syndromes is not examined. It must also be noted that not all patients in our cohort with somatoform

pain disorder could concurrently be 'labeled' as suffering from a functional pain syndrome. It seems as though in the field of functional musculoskeletal pain syndromes, pertinent 'labels' are still lacking. If, however, the new preliminary fibromyalgia criteria 2010 of the American College of Rheumatology, which subsumes more localized musculoskeletal pain syndromes under fibromyalgia prevails, this gap will be closed soon [15,16].

In view of the current revisions of diagnostic systems (DSM-V and ICD-11), continuing with a parallel diagnostic coding system cannot be the way forward in the psychiatric concept of these pain disorders [17,18]. The input of psychiatry has to be different. In addition to treating psychiatric comorbidities, the essential contribution of psychiatry lies in its broader view and recognition of the fact that life experiences in an individual's biography plays a role in pain sensitization. As early as in the 1950s, it was postulated that child distress is associated with an increased incidence of chronic pain disorders [19]. A recent study showed that somatosensory pain susceptibility is increased in young rats separated from their mothers [20]. Today, life stress and traumatization in a person's life history are generally recognized as established pro-nociceptive risk factors. There is ample evidence in the literature showing an association between childhood neglect, experience of violence, and overactive life style, on the one hand and development of the fibromyalgia syndrome, on the other [21-23]. In a rat model it was recently shown that stress hormones induce a switch of intracellular signaling in the primary afferent nociceptive nerve fibers resulting in hyperalgesia [24]. Integrating these (epigenetically determinative) life stress aspects into a broader conceptual understanding will continue to be an important task of psychiatric medicine. It is important for psychiatry to recognize the biological aspect of somatosensory hyperalgesia as a concrete, real fact. Hyperalgesia is not only clinically easily objectified – in our experience it often also proves helpful in an educational context to help patients to get a better understanding of their disorder. In contrast to the traditional, interpreting concept of somatization, patients hardly ever offer resistance against this approach and its contextualization with life stress. Besides taking a detailed psychosocial history, it is also current practice at our clinic to assess the aspect of hyperalgesia in each patient with a 'somatoform-functional' pain disorder. The concept of 'non-organic pain' needs definitively to be abandoned [25].

Abbreviations: HADS-D = Hospital Anxiety and Depression Scale; CRPS = Complex Regional Pain Syndrome; IQR = interquartile range; NRS = numerical pain rating scale; PPdt = pressure pain detection threshold; SD = standard deviation; SE = standard error

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Table 1 : Overview about recent articles on pain processing in somatoform pain disorders

Authors	Main message
Stoeter P et al, *NeuroImage 2007* [26]:	Patients with somatoform pain disorder show altered cerebral activation exposed to pin-prick pain and stress (fMRI study).
Gündel H et al, *Pain 2008* [27]:	Patients with somatoform pain disorder show altered cerebral response to noxious heat stimulation (fMRI study).
Valet M et al, *Psychosom Med 2009* [28]:	Patients with chronic pain disorder show gray-matter loss in pain processing structures (voxel-based morphometric study).

Pollatos O et al,	Pain pressure sensitivity in somatoform patients correlates with depression score
Pain 2011 [29]:	and depends on sympathovagal influences.
Hennings A et al,	Pain pressure sensitivity in patients with depression and multiple somatoform symptoms
Clin J Pain 2012 [14]:	is associated with depression and decreases by physical activity.
Busch V et al,	Sleep deprivation in chronic somatoform pain disorders leads to significantly increased
Psychiatry Res 2012 [30]:	clinical pain complaints but unaltered experimental pain perception (pressure and temperature).

Table 2: Patient Characteristics

			Somatoform pain disorder (all)	Somatoform pain disorder with FPS	Somatoform pain disorder without FPS	Nociceptive pain (all)	Nociceptive pain traumatic	Nociceptive pain degenerative
			n=67	n=41	n=26	n=53	n=27	n=26
Gender	Female		59.7% (40)	63.4% (26)	53.8% (14)	32.1% (17)	22.2% (6)	42.3% (11)
Age (years)	Mean (SD)		46.5 (11.9)	48.0 (12.8)	44.3 (10.2)	55.2 (17.0)	45.4 (14.4)	65.5 (12.9)
		Median (interquartile)	48.0 (40.0–54.0)	49.0 (41.5–56.0)	47.5 (35.8–51.5)	55.0 (44.0–71.5)	44.0 (33.0–52.0)	68.5 (57.0–75.0)
Baseline pain at rest	Mean (SD)		6.3 (2.2)	6.5 (2.0)	5.9 (2.6)	3.5 (1.4)	3.7 (1.5)	3.3 (1.3)
		Median (interquartile)	7.0 (5.0–8.0)	7.0 (6.0–8.0)	6.5 (3.8–8.0)	3.0 (2.0–4.0)	3.0 (3.0–5.0)	3.0 (2.0–4.0)
Duration of pain (months)	Mean (SD)		99.1 (114.4)	102.2 (108.5)	94.3 (125.2)	15.8 (23.2)	4.7 (7.1)	27.2 (28.2)
		Median (interquartile)	55.0 (19.0–120.0)	48.0 (20.0–186.0)	59.0 (18.0–96.0)	6.0 (0.8–23.5)	1.0 (0.3–6.0)	14.0 (4.5–51.0)
Antidepressant drugs			85.1% (57)	87.8% (36)	80.8% (21)	0	0	0
Depression			85.1% (57)	92.7% (38)	19 (73.1%)	0	0	0
Current mood[1)]	Mean (SD)		6.2 (2.7)	6.1 (2.4)	6.3 (3.0)	3.8 (1.6)	3.9 (1.5)	3.8 (1.7)
		Median (interquartile)	6.0 (4.0–8.0)	6.0 (4.5–8.0)	7.5 (4.0–9.0)	4.0 (3.0–4.5)	4.0 (3.0–5.0)	4.0 (3.0–4.3)

FPS= Functional pain syndrome

[1)] Higher scores indicate more negative mood (numerical rating scale, range 0-10)

Table 3: Pain Sensitivity Data of the Compared Groups

					95% Confidence Interval for Mean	
Algometry test	**Patients**	**Mean**	**SD**	**SE**	**Lower Bound**	**Upper Bound**
	Somatoform pain disorders (all)	152.5	93.4	11.4	129.7	175.3
Electronic	With FPS	149.4	100.4	15.7	117.7	181.0
Algometer	Without FPS	157.5	82.7	16.2	124.1	190.9
(PPdt, kilopascal)	**Nociceptive (all)**	217.5	78.0	10.7	196.0	239.0
Middle finger[1)]	Traumatic	243.2	80.6	15.5	211.3	275.1
	Degenerative	190.8	66.6	13.1	163.9	217.8
Peg Algometer	**Somatoform pain disorders (all)**	4.2	2.8	0.3	3.5	4.9
(NRS score, 0–10)	With FPS	4.6	2.9	0.5	3.7	5.6
Middle finger[1)]	Without FPS	3.6	2.5	0.5	2.6	4.6
	Nociceptive (all)	1.7	1.0	0.1	1.4	2.0
	Traumatic	1.5	0.9	0.2	1.1	1.8
	Degenerative	1.9	1.1	0.2	1.5	2.4

Peg Algometer	**Somatoform pain disorders (all)**	7.2	2.4	0.3	6.7	7.8
(NRS score, 0–10)	With FPS	7.4	2.5	0.4	6.6	8.2
Earlobe[2)]	Without FPS	7.0	2.3	0.5	6.0	7.9
	Nociceptive (all)	4.2	1.6	0.2	3.7	4.6
	Traumatic	3.9	1.4	0.3	3.3	4.4
	Degenerative	4.5	1.7	0.3	3.8	5.2

FPS= Functional pain syndrome

NRS= Numerical rating scale

PPdt= Pressure pain detecting threshold

[1)] Mean value of left and right middle fingers

[2)] Mean value of left and right earlobes

Fig.1 **Pain syndromes not sufficiently explained with peripheral leasons or neuropathic terms**

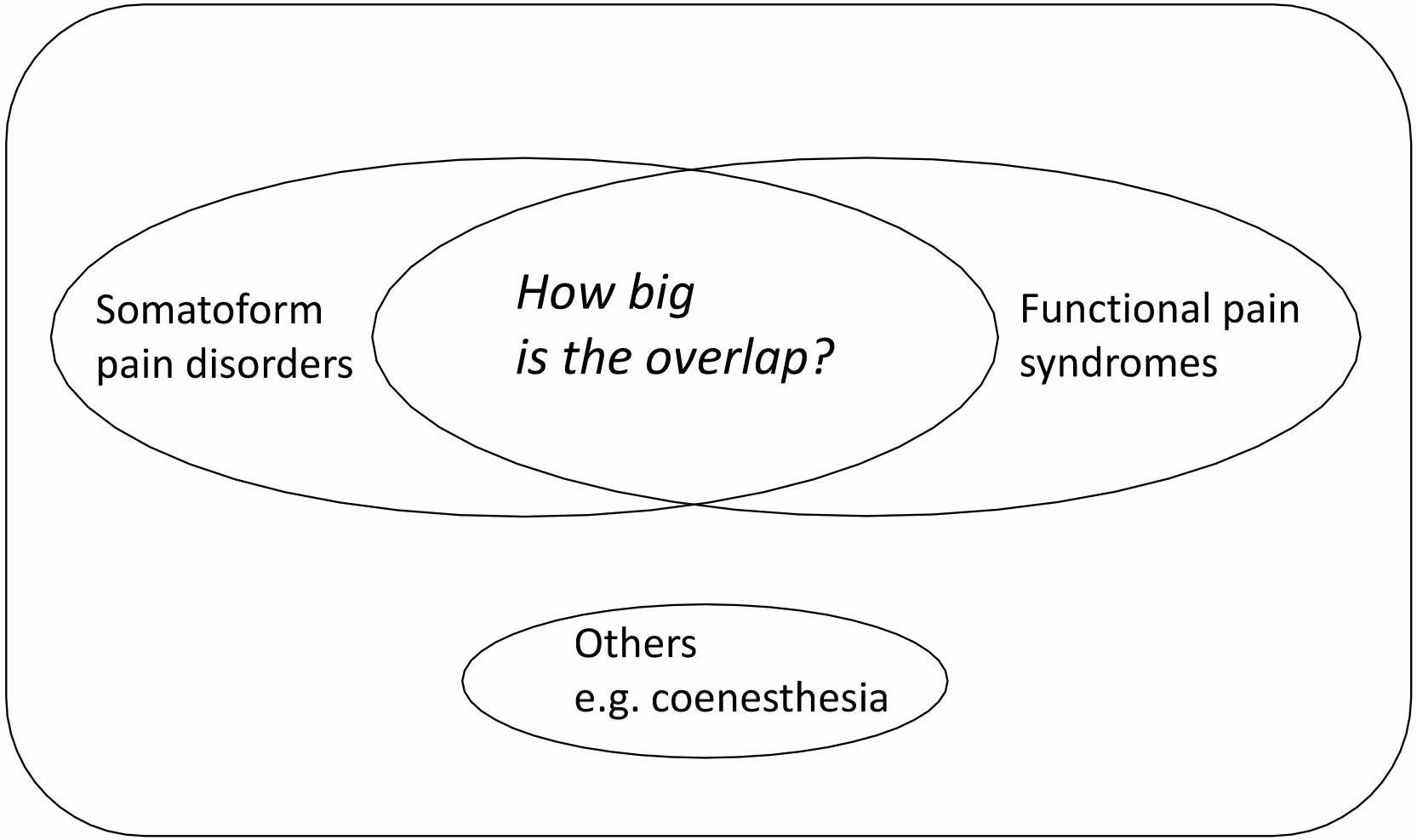
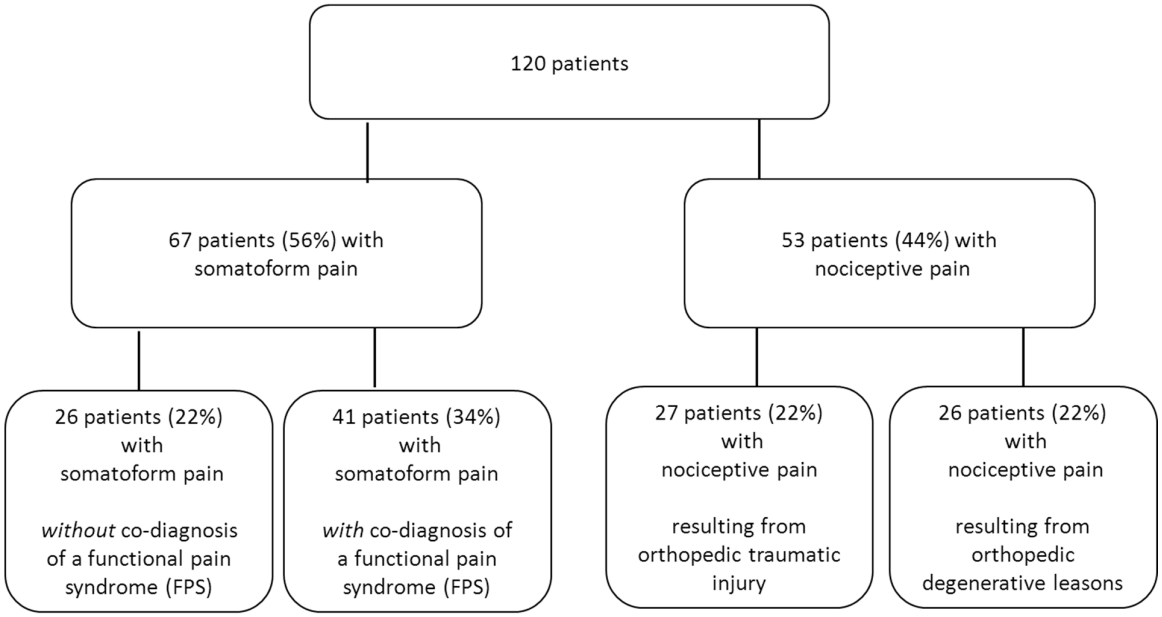
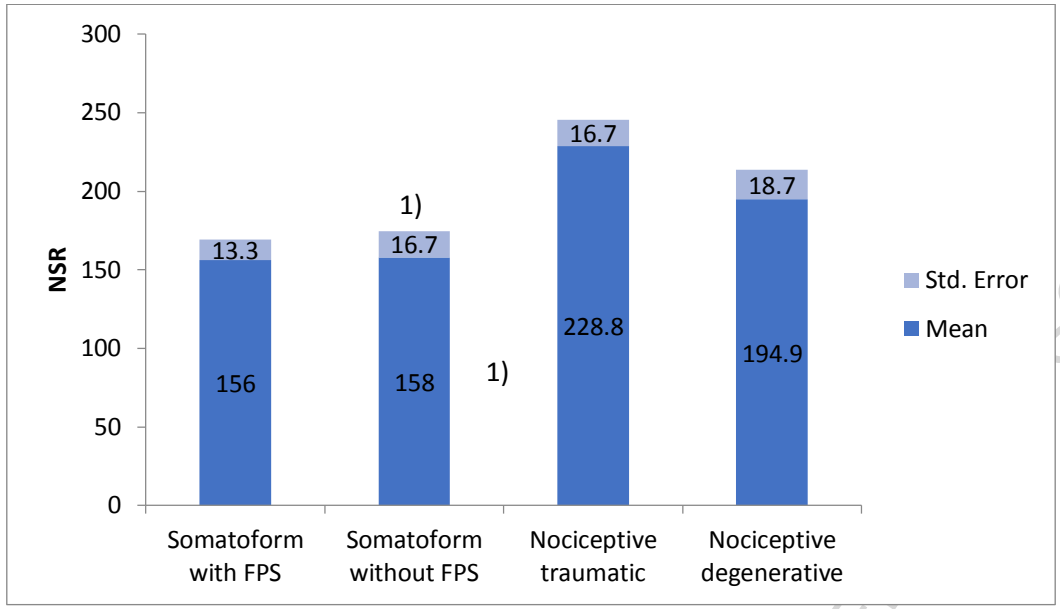


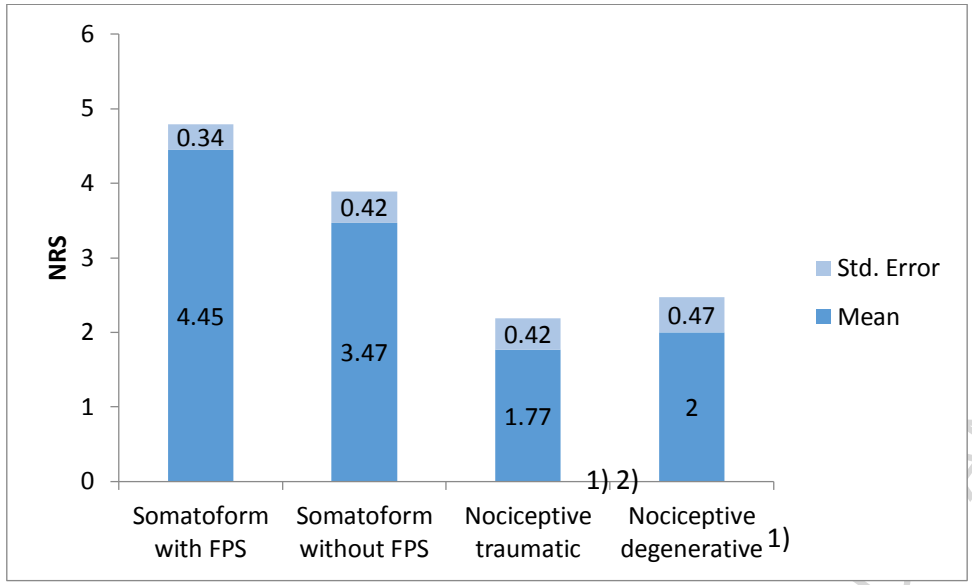
Fig.2 **Flowchart**





Standard Error

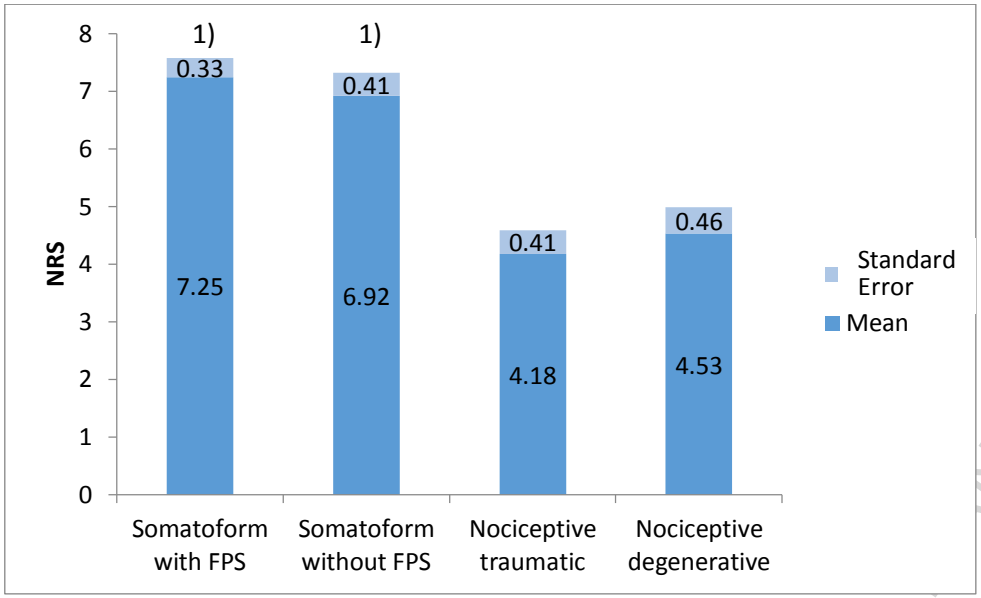
1) Significant differences in comparison with the *traumatic nociceptive* subgroup, corresponding with the definition of *hypersensitivity* (p-values < 0.004).
Controlled for age and gender
FPS = Functional pain syndrome
NRS= Numeric rating scale



Standard Error

1) Significant differences in comparison with the *traumatic nociceptive* subgroup, corresponding with the definition of *hyperalgesia* (p-values < 0.008).
2) Significant difference in comparison with the *degenerative nociceptive subgroup* corresponding with the definition of *hyperalgesia* (p = 0.004).

Controlled for age and gender
FPS = Functional pain syndrome
NRS= Numeric rating scale



1) Significant differences in comparison with *each of the nociceptive* subgroups, corresponding with the definition of *hyperalgesia* (p-values < 0.001).
Controlled for age and gender
FPS = Functional pain syndrome
NRS= Numeric rating scale